REMARKS

I. Comments on Restriction Requirement

The Examiner attempted to justify the requiring Applicants to choose one among SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5 by alleging that "the sequences presented in claims 1, 2, 16, and 17 are considered as independent and distinct inventions, not species, since SEQ ID NO:1, 3, and 5 describe three different proteins with different structures and modes of action." (Office Action, page 2.) Applicants submit that the Examiner's allegation that having "independent and distinct inventions" causes this not to be a "species" election clearly contravenes the procedure outlined in the MPEP for examination of Markush-type claims. The MPEP states that even if a Markush-type claim includes independent and distinct inventions, "the examiner may require a provisional election of a single **species**." (8th edition of the M.P.E.P. (August 2001) at § 803.02, emphasis added.)

In addition, Applicants submit that examination of all three sequences (SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5) in the instant application would not be an undue burden on the Examiner. In the previous two applications to which the instant case claims priority (United States patent application Serial No. 09/368,408 filed on August 4, 1999, which was itself a divisional application of and claimed priority to United States patent application Serial No. 08/967,364 filed on November 7, 1997), claims to multiple sequences were examined together. In United States patent application Serial No. 08/967,364, claims to polynucleotides encoding SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5 were examined and allowed. In United States patent application Serial No. 09/368,408, claims to methods of detecting polynucleotides encoding SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5 were examined and allowed. The apparent lack of burden on the Examiner in these parent applications, as well as the availability to the instant Examiner of the results of searches already made by the Examiner in the previous two applications, suggest that there would be no undue burden on instant Examiner to examine claims to SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5 in the present application.

For at least the above reasons, Applicants request reconsideration of the Restriction Requirement and examination of Claims 1, 2, 16, and 17 with respect to SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5.

II. Summary of Invention

Applicants' invention is directed, *inter alia*, to polypeptides having strong homology to mouse vacuolar protein sorting homolog (GI 1703494) ("VTP-1") and compositions containing them, which have a variety of utilities, in particular in expression profiling, and in particular for diagnosis of conditions or diseases characterized by expression of VTP-1, for toxicology testing, and for drug discovery (see the Specification at, e.g., page 38, lines 22-30, and page 45, line 20 through page 46, line 7). As described in the Specification:

> Nucleic acids encoding the VTP-1 of the present invention were first identified in Incyte Clone 75871 from a THP-1 cell line cDNA library (THP1PEB01) using a computer search for amino acid sequence alignments. A consensus sequence, SEQ ID NO:2, was derived from the following overlapping and/or extended nucleic acid sequences: Incyte Clones 1396925 (BRAITUT08), 100797 (ADRENOT01), and 75871 (THP1PEB01).
>
> In one embodiment, the invention encompasses a polypeptide, VTP-1, comprising the amino acid sequence of SEQ ID NO:1, as shown in Figures 1A, 1B, 1C, 1D, 1E, 1F, and 1G. VTP-1 is 570 amino acids in length. VTP-1 has one potential amidation site encompassing residues G430-R433; one potential N-glycosylation sites encompassing residues N522-T525; one potential cAMP- and cGMP-dependent protein kinase phosphorylation site encompassing residues K322-S325; 10 potential casein kinase II phosphorylation sites encompassing residues T40-E43, S103-D106, S109-E112, S307-D310, S351-E354, T380-D383, S441-D444, T494-D497, T511-E514, and S542-E545; and seven potential protein kinase C phosphorylation sites encompassing residues S168-K170, S343-R345, S416-K418, S441-K443, T494-R496, T563-R565, and S568-R570. As shown in Figures 2A and 2B, VTP-1 has chemical and structural homology with a mouse vacuolar protein-sorting protein, mVps45 (GI 1703494; SEQ ID NO:7). In particular, VTP-1 and mVps45 share 97% sequence homology. As illustrated by Figures 3A and 3B, VTP-1 and Vps45 have rather similar hydrophobicity plots. Northern analysis shows the expression of VTP-1 in various cDNA libraries, at least 42% of which are immortalized or cancerous, at least 24% of which involve immune response, and at least 29% are expressed in fetal/infant tissues or organs. (Specification, page 14, line 12 through page 15, line 2.)

III. Rejection of Claims 1, 2, 16, and 17 Under 35 U.S.C. § 101

Claims 1, 2, 16, and 17 stand rejected under 35 U.S.C. § 101 based on the allegation that the claimed invention lacks patentable utility. The rejection alleges in particular that the

invention is not "supported by either specific and/or substantial utility or a well established utility." (Office Action, page 6.)

The rejection of claims 1, 2, 16, and 17 is improper, as the inventions of those claims have a patentable utility as set forth in the instant specification, and/or a utility well-known to one of ordinary skill in the art.

The invention at issue, identified in the patent application as vesicle trafficking protein-1, abbreviated as VTP-1, is a polypeptide sequence encoded by a gene that is expressed in a human THP-1 cell line. The novel polypeptide is demonstrated in the specification to be a member of the class of vps45-related vesicle trafficking proteins, whose biological functions include mediating transport among the Golgi complex, synaptic vesicles, prelysosomal compartments, and the lysosome. (Specification, page 2, lines 2-4.) As such, the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which require knowledge of how the polypeptide actually functions. As a result of the benefits of these uses, the claimed invention already enjoys significant commercial success.

The similarity of the claimed polypeptide to another polypeptide of known, undisputed utility by itself demonstrates utility beyond the reasonable probability required by law. VTP-1 is, in that regard, homologous to mouse vacuolar protein-sorting homolog (mVps45; GI 1703494) . mVps45 is a mammalian homolog to a yeast protein, Vps45, which "is essential for transport from the Golgi to a prevacuolar compartment." (Specification, page 1.) The Bandman '178 specification teaches that mammalian homologs to yeast vesicle trafficking proteins "are essential in mediating transport among the Golgi complex, synaptic vesicles, prelysosomal compartments, and the lysosome." (Specification, page 2, lines 2-4.) The Pevsner article (incorporated by reference into the Specification; Tab H) states that:

> A description of the proteins involved in lysosomal targeting is essential to understand lysosomal function in the biosynthetic and endocytic pathways, and also to understand diseases involving lysosomes. Protein trafficking to lysosomes may be disrupted in neurodegenerative disorders such as Alzheimer's disease and prion encephalopathies (Mayer et al., 1992; Cataldo et al., 1994) as well as organelle storage disorders diseases such as Chediak-Higashi syndrome (Zhao et al., 1994). (Tab H, page 14)

In particular, the two polypeptides share 97% sequence identity over 570 amino acid residues. In addition, "[a]s illustrated by Figures 3A and 3B, VTP-1 and Vps45 have rather similar hydrophobicity plots." (Specification, page 14, lines 28-30.)

This is more than enough homology to demonstrate a reasonable probability that the utility of mVps45 can be imputed to the claimed invention. It is well-known that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small. (Brenner et. al., Proc. Natl. Acad. Sci. U.S.A. 95:6073-78 (1998); Reference No. 1). Given homology in excess of 40% over many more than 70 amino acid residues, the probability that the claimed polypeptide is related to mVps45 is, accordingly, very high.

There is, in addition, direct proof of the utility of the claimed invention. Applicants submit with this Response the Declaration of L. Michael Furness describing some of the practical uses of the claimed invention in gene and protein expression monitoring applications as they would have been understood at the time of the patent application. The Furness Declaration describes, in particular, how the claimed polypeptide can be used in protein expression analysis techniques such as 2-D PAGE gels and western blots. Using the claimed invention with these techniques, persons of ordinary skill in the art can better assess, for example, the potential toxic affect of a drug candidate. (Furness Declaration at ¶ 10).

The Patent Examiner contends that the claimed polypeptide cannot be useful without precise knowledge of its function. But the law never has required knowledge of biological function to prove utility. It is the claimed invention's uses, not its functions, that are the subject of a proper analysis under the utility requirement.

In any event, as demonstrated by the Furness Declaration, the person of ordinary skill in the art can achieve beneficial results from the claimed polypeptide in the absence of any knowledge as to the precise function of the protein. The uses of the claimed polypeptide for gene expression monitoring applications including toxicology testing are in fact independent of its precise function.

A. The Applicable Legal Standard

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent

applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not

make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

B. The uses of VTP-1 for toxicology testing, drug discovery, and disease diagnosis are sufficient utilities under 35 U.S.C. §§ 101 and 112, first paragraph

The claimed invention meets all of the necessary requirements for establishing a credible utility under the Patent Law: There are "well-established" uses for the claimed invention known to persons of ordinary skill in the art, and there are specific practical and beneficial uses for the invention disclosed in the patent application's specification. These uses are explained, in detail, in the Furness Declaration accompanying this Response. Objective evidence, not considered by the Patent Office, further corroborates the credibility of the asserted utilities.

1. The claimed polypeptide's membership in the Vps45-related protein family demonstrates utility.

It is undisputed, and readily apparent from the patent application, that the claimed polypeptide shares 97% sequence identity over 570 amino acid residues with mVps45. In addition, "[a]s illustrated by Figures 3A and 3B, VTP-1 and Vps45 have rather similar hydrophobicity plots." (Specification, page 14, lines 28-30.) This is more than enough

homology to demonstrate a reasonable probability that the utility of mVps45 can be imputed to the claimed invention. It is well-known that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small. Brenner et. al., Proc. Natl. Acad. Sci. U.S.A. 95:6073-78 (1998) (Reference No. 1). Given homology in excess of 40% over many more than 70 amino acid residues, the probability that the claimed polypeptide is related to mVps45 is, accordingly, very high.

Because there is a substantial likelihood that the claimed VTP-1 is a member of the Vps45-related family of polypeptides, the members of which are indisputably useful (the Examiner's unsupported doubt of which is noted, but is not dispositive), there is by implication a substantial likelihood that the claimed polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. *In re Brana*, 51 F.3d at 1567.

(For the record, the Examiner's citation of statements in the 1996 Pevsner article using the term "may" in describing the functional properties of the protein rather than more positive statements reflects the conservative vocabulary of peer-reviewed papers and not actual doubt on the part of the authors.)

It is undisputed that the claimed polypeptide is a protein having the sequence shown as SEQ ID NO:1 in the patent application and referred to as VTP-1 in that application. Applicants have demonstrated by more than reasonable probability that VTP-1 is a member of the Vps45-related family of polypeptides, and that the Vps45-related family of polypeptides mediate transport among the Golgi complex, synaptic vesicles, prelysosomal compartments, and the lysosome.

While the Examiner has cited literature (Gerhold et al., Wells et al., and Russell et al.) identifying some of the difficulties that may be involved in predicting protein function, none suggest that functional homology cannot be inferred by a reasonable probability in this case. Importantly, none contradict Brenner's basic teaching that sequence homology in excess of 40% over 70 or more amino acid residues yields a high probability of functional homology as well. At most, these articles individually and together stand for the proposition that it is difficult to make predictions about function with certainty. The standard applicable in this case is not, however, proof to certainty, but rather proof to reasonable probability.

The Examiner asserts that the sequence similarity between VTP-1 and a human Vps45

homolog (assumed to be the Pevsner et al. sequence, but not listed explicitly as such by the Examiner) is not adequate to allow one to attribute the function of the Pevsner human Vps45 protein to VTP-1. (It is noted that the Examiner never discusses the mouse homolog that is described in the Figures 2A and 2B, Figure 3B, and in the Specification, presumably because the paper disclosing the mouse sequence, Tellam, J.T., et al., "Identification of a Mammalian Golgi Sec1p-like Protein, mVps45," (March 7, 1997) J. Biol. Chem. 272:6187-6193 (Reference No. 2) does not share these purported defects.) The Examiner alleges that:

> Absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases. (Office Action, pages 7-8.)

In support of these assertions, the Examiner refers to publications by Gerhold et al., Wells et al., and Russell et al.

Applicants respectfully point out that the cited references do not appear to support the Examiner's position. In the paper by Russell et al., for example, while the focus is on the conservation of protein folds rather than function, the authors do mention that "both the sequence and structure of similar proteins can evolve beyond recognition even when function is conserved." (Russell et al., page 348, column 1.) The paper by Gerhold et al. notes that homologs of human genes in organisms as diverse as fruit flies, worms, and yeast have proven to be useful in determining the functions of the human genes (see Gerhold et al, page 979). The paper by Wells et al. discloses that it is possible to identify novel members of the chemokine family "even though the overall sequence identity levels between chemokines may be as low as

20%" (Wells et al., page 546, column 1). Thus the known art clearly demonstrates that evolutionarily related proteins may exhibit considerable divergence in sequence while conserving the same overall three-dimensional structure and function. In addition, natural selection will tend to act against random mutations that alter protein structure as these would destroy or diminish protein function; such non-functional mutated proteins will frequently result in lethal mutations and will, therefore, be selected against and eliminated from the gene-pool. One of skill in the art would therefore clearly understand that sequence similarities of far less than 100% may be reliably used to determine protein function.

The Examiner referenced the Revised Interim Utility Guidelines Training Materials in support of the rejection. Applicants submit that both the Revised Interim Utility Guidelines and the Revised Interim Utility Guidelines Training Materials support the use of sequence homology to known proteins to establish functional homology. The Revised Interim Utility Guidelines specifically state at page 1096, that the Examiner's decision to rebut Applicants assertion of utility:

> ---must be supported by a preponderance of all evidence of record. More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient". (emphasis added).

Clearly the PTO recognizes the well known use of sequence homology in the art to establish protein function. The Revised Interim Utility Guidelines Training Materials elaborate further on this matter in Example 10:DNA Fragment encoding a Full Open Reading Frame (ORF) at page 53, which recites a claim to a nucleic acid encoding a protein with 95% sequence identity to a known protein (a DNA ligase). The example clearly states that "there is no reason to doubt the assertion that [the claimed sequence] encodes a DNA ligase." Therefore the Revised Interim Utility Guidelines Training Materials indicate that a sequence similarity of less than 100% is deemed reasonably to support to one skilled in the art that two molecules could possess the same activity.

The Examiner's citation of Gerhold et al. and Wells et al. with respect to the

unpredictability of predicting function from sequence homology is irrelevant to the instant situation. Both references relate to the use of ESTs (fragments of genes) to predict full-length genes and their open reading frames. This does not relate to the current situation in which the polynucleotides (encoding the claimed polypeptides) are full length genes whose identity to other full length genes is based on a high degree of sequence similarity to one another.

The Examiner must accept the applicant's demonstration that the claimed polypeptide is a member of Vps45-related protein family and that utility is proven by a reasonable probability unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). The Examiner has not provided sufficient evidence or sound scientific reasoning to the contrary.

Nor has the Examiner provided any evidence that any member of the Vps45-related protein family, let alone a substantial number of those members, is not useful. In such circumstances the only reasonable inference is that the claimed polypeptide must be, like the other members of the Vps45-related protein family, useful.

2. The uses of VTP-1 for toxicology testing, drug discovery, and disease diagnosis are practical uses that confer "specific benefits" to the public

The claimed invention has specific, substantial, real-world utility by virtue of its use in toxicology testing, drug development and disease diagnosis through gene expression profiling. These uses are explained in detail in the accompanying Furness Declaration, the substance of which is not rebutted by the Patent Examiner. There is no dispute that the claimed invention is in fact a useful tool in two-dimensional polyacrylamide gel electrophoresis ("2-D PAGE") analysis and western blots used to monitor protein expression and assess drug toxicity.

The instant application (the Bandman '178 application) is a divisional of, and claims priority to, to United States patent application Serial No. 09/368,408 filed on August 4, 1999, which was itself a divisional application of and claimed priority to United States patent application Serial No. 08/967,364 filed on November 7, 1997 (hereinafter "the Bandman '364 application") having essentially the identical specification, with the exception of corrected

typographical errors and reformatting. Thus page and line numbers may not match as between the Bandman '178 application and the Bandman '364 application.

In his Declaration, Mr. Furness explains the many reasons why a person skilled in the art who read the Bandman '364 application on November 7, 1997 would have understood that application to disclose the claimed polypeptide to be useful for a number of gene and protein expression monitoring applications, *e.g.*, in 2-D PAGE technologies, in connection with the development of drugs and the monitoring of the activity of such drugs. (Furness Declaration at, e.g., ¶¶ 7-13). Much, but not all, of Mr. Furness' explanation concerns the use of the claimed polypeptide in the creation of protein expression maps using 2-D PAGE.

2-D PAGE technologies were developed during the 1980's. Since the early 1990's, 2-D PAGE has been used to create maps showing the differential expression of proteins in different cell types or in similar cell types in response to drugs and potential toxic agents. Each expression pattern reveals the state of a tissue or cell type in its given environment, *e.g.*, in the presence or absence of a drug. By comparing a map of cells treated with a potential drug candidate to a map of cells not treated with the candidate, for example, the potential toxicity of a drug can be assessed. (Furness Declaration at ¶ 12.)

The claimed invention makes 2-D PAGE analysis a more powerful tool for toxicology and drug efficacy testing. A person of ordinary skill in the art can derive more information about the state or states or tissue or cell samples from 2-D PAGE analysis with the claimed invention than without it. As Mr. Furness explains:

> In view of the Bandman '364 application, . . . and other related pre-November 7, 1997 publications, persons skilled in the art on November 7, 1997 clearly would have understood the Bandman '364 application to disclose the SEQ ID NO:1 polypeptide to be useful in 2-D PAGE analyses for the development of new drugs and monitoring the activities of drugs for such purposes as evaluating their efficacy and toxicity . . . (Furness Declaration, ¶ 10)
>
> * * *
>
> Persons skilled in the art would appreciate that a 2-D PAGE map that utilized the SEQ ID NO:1 polypeptide sequence would be a more useful tool than a 2-D PAGE map that did not utilize this protein sequence in connection with conducting protein expression monitoring studies on proposed (or actual) drugs for treating inflammation and disorders associated with cell proliferation and apoptosis for such purposes as evaluating their efficacy and toxicity (Furness Declaration, ¶ 12)

Mr. Furness' observations are confirmed in the literature published before the filing of the patent application. Wilkins, for example, describes how 2-D gels are used to define proteins present in various tissues and measure their levels of expression, the data from which is in turn used in databases:

> For proteome projects, the aim of [computer-aided 2-D PAGE] analysis . . . is to catalogue all spots from the 2-D gel in a qualitative and if possible quantitative manner, so as to define the number of proteins present and their levels of expression. Reference gel images, constructed from one or more gels, for the basis of two-dimensional gel databases. (Wilkins, Tab C, page 26).

3. The use of proteins expressed by humans as tools for toxicology testing, drug discovery, and the diagnosis of disease is now "well-established"

The technologies made possible by expression profiling using polypeptides are now well-established. The technical literature recognizes not only the prevalence of these technologies, but also their unprecedented advantages in drug development, testing and safety assessment. These technologies include toxicology testing, as described by Furness in his Declaration.

Toxicology testing is now standard practice in the pharmaceutical industry. See, *e.g.*, John C. Rockett, et. al., Differential gene expression in drug metabolism and toxicology: practicalities, problems, and potential, Xenobiotica 29:655-691 (July 1999) (Reference No. 3):

> Knowledge of toxin-dependent regulation in target tissues is not solely an academic pursuit as much interest has been generated in the pharmaceutical industry to harness this technology in the early identification of toxic drug candidates, thereby shortening the developmental process and contributing substantially to the safety assessment of new drugs. ((Reference No. 3), page 656)

To the same effect are several other scientific publications, including Emile F. Nuwaysir, et al., Microarrays and Toxicology: The Advent of Toxicogenomics, Molecular Carcinogenesis 24:153-159 (1999) (Reference No. 4); Sandra Steiner and N. Leigh Anderson, Expression profiling in toxicology -- potentials and limitations, Toxicology Letters 112-13:467-471 (2000) (Reference No. 5).

The more genes – and, accordingly, the polypeptides they encode -- that are available for

use in toxicology testing, the more powerful the technique. Control genes are carefully selected for their stability across a large set of array experiments in order to best study the effect of toxicological compounds. See attached email from the primary investigator, Dr. Cynthia Afshari to an Incyte employee, dated July 3, 2000, as well as the original message to which she was responding (Reference No. 6) Thus, there is no expressed gene which is irrelevant to screening for toxicological effects, and all expressed genes have a utility for toxicological screening.

In fact, the potential benefit to the public, in terms of lives saved and reduced health care costs, are enormous. Recent developments provide evidence that the benefits of this information are already beginning to manifest themselves. Examples include the following:

- In 1999, CV Therapeutics, an Incyte collaborator, was able to use Incyte gene expression technology, information about the structure of a known transporter gene, and chromosomal mapping location, to identify the key gene associated with Tangier disease. This discovery took place over a matter of only a few weeks, due to the power of these new genomics technologies. The discovery received an award from the American Heart Association as one of the top 10 discoveries associated with heart disease research in 1999.

- In an April 9, 2000, article published by the Bloomberg news service, an Incyte customer stated that it had reduced the time associated with target discovery and validation from 36 months to 18 months, through use of Incyte's genomic information database. Other Incyte customers have privately reported similar experiences. The implications of this significant saving of time and expense for the number of drugs that may be developed and their cost are obvious.

- In a February 10, 2000, article in the *Wall Street Journal*, one Incyte customer stated that over 50 percent of the drug targets in its current pipeline were derived from the Incyte database. Other Incyte customers have privately reported similar experiences. By doubling the number of targets available to pharmaceutical researchers, Incyte genomic information has demonstrably accelerated the development of new drugs.

Because the Patent Examiner failed to address or consider the "well-established" utilities for the claimed invention in toxicology testing, drug development, and the diagnosis of disease, the Examiner's rejections should be withdrawn regardless of their merit.

4. Objective evidence corroborates the utilities of the claimed invention

There is in fact no restriction on the kinds of evidence a Patent Examiner may consider in

determining whether a "real-world" utility exists. "Real-world" evidence, such as evidence showing actual use or commercial success of the invention, can demonstrate conclusive proof of utility. *Raytheon v. Roper*, 220 USPQ2d 592 (Fed. Cir. 1983); *Nestle v. Eugene*, 55 F.2d 854, 856, 12 USPQ 335 (6th Cir. 1932). Indeed, proof that the invention is made, used or sold by any person or entity other than the patentee is conclusive proof of utility. *United States Steel Corp.* v. *Phillips Petroleum Co.*, 865 F.2d 1247, 1252, 9 USPQ2d 1461 (Fed. Cir. 1989).

Over the past several years, a vibrant market has developed for databases containing all expressed genes (along with the polypeptide translations of those genes). (Note that the value in these databases is enhanced by their completeness, but each sequence in them is independently valuable.) The databases sold by Applicants' assignee, Incyte, include exactly the kinds of information made possible by the claimed invention, such as tissue and disease associations. Incyte sells its database containing the claimed sequence and millions of other sequences throughout the scientific community, including to pharmaceutical companies who use the information to develop new pharmaceuticals.

Both Incyte's customers and the scientific community have acknowledged that Incyte's databases have proven to be valuable in, for example, the identification and development of drug candidates. As Incyte adds information to its databases, including the information that can be generated only as a result of Incyte's discovery of the claimed polypeptide, the databases become even more powerful tools. Thus the claimed invention adds more than incremental benefit to the drug discovery and development process.

C. The Patent Examiner's Rejections Are Without Merit

Rather than responding to the evidence demonstrating utility, the Examiner attempts to dismiss it altogether by arguing that the disclosed and well-established utilities for the claimed polypeptide are not "specific and/or substantial" or "well-established" utilities. (Office Action at page 6.) The Examiner is incorrect both as a matter of law and as a matter of fact.

1. The Precise Biological Role Or Function Of An Expressed Polypeptide Is Not Required To Demonstrate Utility

The Patent Examiner's primary rejection of the claimed invention is based on the ground

that, without information as to the precise "biological role" of the claimed invention, the claimed invention's utility is not sufficiently specific. According to the Examiner, it is not enough that a person of ordinary skill in the art could use and, in fact, would want to use the claimed invention either by itself or in a 2-D gel or western blot to monitor the expression of genes for such applications as the evaluation of a drug's efficacy and toxicity. The Examiner would require, in addition, that the applicant provide a specific and substantial interpretation of the results generated in any given expression analysis.

It may be that specific and substantial interpretations and detailed information on biological function are necessary to satisfy the requirements for publication in some technical journals, but they are not necessary to satisfy the requirements for obtaining a United States patent. The relevant question is not, as the Examiner would have it, whether it is known how or why the invention works, *In re Cortwright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999), but rather whether the invention provides an "identifiable benefit" in presently available form. *Juicy Whip Inc.* v. *Orange Bang Inc.*, 185 F.3d 1364, 1366 (Fed. Cir. 1999). If the benefit exists, and there is a substantial likelihood the invention provides the benefit, it is useful. There can be no doubt, particularly in view of the Furness Declaration (at, *e.g.*, ¶¶ 10-13), that the present invention meets this test.

The threshold for determining whether an invention produces an identifiable benefit is low. *Juicy Whip*, 185 F.3d at 1366. Only those utilities that are so nebulous that a person of ordinary skill in the art would not know how to achieve an identifiable benefit and, at least according to the PTO guidelines, so-called "throwaway" utilities that are not directed to a person of ordinary skill in the art at all, do not meet the statutory requirement of utility. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

Knowledge of the biological function or role of a biological molecule has never been required to show real-world benefit. In its most recent explanation of its own utility guidelines, the PTO acknowledged as much (66 F.R. at 1095):

> [T]he utility of a claimed DNA does not necessarily depend on the function of the encoded gene product. A claimed DNA may have specific and substantial utility because, *e.g.*, it hybridizes near a disease-associated gene or it has gene-regulating activity.

By implicitly requiring knowledge of biological function for any claimed polypeptide, the

Examiner has, contrary to law, elevated what is at most an evidentiary factor into an absolute requirement of utility. Rather than looking to the biological role or function of the claimed invention, the Examiner should have looked first to the benefits it is alleged to provide.

2. Membership in a Class of Useful Products Can Be Proof of Utility

Despite the uncontradicted evidence that the claimed polypeptide is a member of both the Vps45-related protein family and the family of expressed polypeptides, whose members indisputably are useful, the Examiner refused to impute the utility of the members of the Vps45-related protein family and the family of expressed polypeptides to VTP-1. In the Office Action, the Patent Examiner takes the position that unless Applicants can identify which particular biological function within the class of Vps45-related proteins or expressed polypeptides is possessed by VTP-1, utility cannot be imputed. And, without sufficient evidence or sound scientific reasoning, the Examiner apparently does not believe that the prior art has even established a utility for this well-characterized class of proteins. Further, presumably, to demonstrate any such utility by membership in the class of Vps45-related proteins or expressed polypeptides, the Examiner would require that all Vps45-related proteins or expressed polypeptides possess a "common" utility.

There is no such requirement in the law. In order to demonstrate utility by membership in a class, the law requires only that the class not contain a substantial number of useless members. So long as the class does not contain a substantial number of useless members, there is sufficient likelihood that the claimed invention will have utility and a rejection under 35 U.S.C. § 101 is improper. That is true regardless of how the claimed invention ultimately is used and whether the members of the class possess one utility or many. *See Brenner* v. *Manson*, 383 U.S. 519, 532 (1966); *Application of Kirk*, 376 F.2d 936, 943 (CCPA 1967).

Membership in a "general" class is insufficient to demonstrate utility only if the class contains a substantial number of useless members. There would be, in that case, a substantial likelihood that the claimed invention is one of the useless members of the class. In the few cases in which class membership did not prove utility by substantial likelihood, the classes did in fact include predominately useless members; see, e.g., *Brenner* (man-made steroids); *Kirk* (same);

Natta (man-made polyethylene polymers).[1]

The Examiner addresses VTP-1 as if the general class in which it is included is not the Vps45-related protein family or the family of expressed polypeptides, but rather all polypeptides, including the vast majority of useless theoretical molecules not occurring in nature, and thus not pre-selected by nature to be useful. While these "general classes" may contain a substantial number of useless members, the Vps45-related protein family and the family of expressed polypeptides do not. The Vps45-related protein family and the family of expressed polypeptides are sufficiently specific to rule out any reasonable possibility that VTP-1 would not also be useful like the other members of the family.

Because the Examiner has not presented any evidence that the Vps45-related and expressed classes of polypeptides have any, let alone a substantial number, of useless members, the Examiner must conclude that there is a "substantial likelihood" that the VTP-1 encoded by the claimed polypeptide is useful.

Even if the Examiner's "common utility" criterion were correct – and it is not – the Vps45-related and expressed polypeptide families would meet it. It is undisputed that known members of the Vps45-related protein family mediate transport among the Golgi complex, synaptic vesicles, prelysosomal compartments, and the lysosome.. A person of ordinary skill in the art need not know any more about how the claimed invention mediates transport among the Golgi complex, synaptic vesicles, prelysosomal compartments, and the lysosome. to use it, and the Examiner presents no evidence to the contrary.

As demonstrated by Applicants, knowledge that VTP-1 is a Vps45-related protein and an expressed polypeptide is more than sufficient to make it useful for the diagnosis and treatment of inflammation and disorders associated with cell proliferation and apoptosis. Indeed, VTP-1 has been shown to be expressed in tissues associated with cancer, inflammation, and fetal/infant development. (Specification, page 27, lines 27-29.) The Examiner must accept these facts to be true unless the Examiner can provide evidence or sound scientific reasoning to the contrary.

---

[1]At a recent Biotechnology Customer Partnership Meeting, PTO Senior Examiner James Martinell described an analytical framework roughly consistent with this analysis. He stated that when an applicant's claimed protein "is a member of a family of proteins that already are known based upon sequence homology," that can be an effective assertion of utility.

But the Examiner has not done so.

3. The uses of VTP-1 in toxicology testing, drug discovery, and disease diagnosis are practical uses beyond mere study of the invention itself

There is no authority for the proposition that use as a tool for research is not a substantial utility. Indeed, the Patent Office itself has recognized that just because an invention is used in a research setting does not mean that it lacks utility (Section 2107.01 of the Manual of Patent Examining Procedure, 8th Edition, August 2001, under the heading I. Specific and Substantial Requirements, Research Tools):

> Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the specific invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm.

The PTO's actual practice has been, at least until the present, consistent with that approach. It has routinely issued patents for inventions whose only use is to facilitate research, such as DNA ligases, acknowledged by the PTO's Training Materials to be useful.

The subset of research uses that are not "substantial" utilities is limited. It consists only of those uses in which the claimed invention is to be an **object** of further study, thus merely inviting further research on the invention itself. This follows from *Brenner*, in which the U.S. Supreme Court held that a process for making a compound does not confer a substantial benefit where the only known use of the compound was to be the object of further research to determine its use. *Id.* at 535. Similarly, in *Kirk*, the Court held that a compound would not confer substantial benefit on the public merely because it might be used to synthesize some other, unknown compound that would confer substantial benefit. *Kirk*, 376 F.2d at 940, 945. ("What appellants are really saying to those in the art is take these steroids, experiment, and find what use they do have as medicines.") Nowhere do those cases state or imply, however, that a material cannot be patentable if it has some other, additional beneficial use in research.

Such beneficial uses beyond studying the claimed invention itself have been

demonstrated, in particular those described in the Furness Declaration. The Furness Declaration demonstrates that the claimed invention is a tool, rather than an object, of research, and it demonstrates exactly how that tool is used. Without the claimed invention, it would be more difficult to generate information regarding the properties of tissues, cells, drug candidates and toxins apart from additional information about the polypeptide itself.

The claimed invention has numerous other uses as a research tool, each of which alone is a "substantial utility." These include uses in diagnostics and drug screening (Specification, page 38, lines 13-30 and page 45, line 20 through page 46, line 7.

4. The Patent Examiner Failed to Demonstrate That a Person of Ordinary Skill in the Art Would Reasonably Doubt the Utility of the Claimed Invention

Based principally on citations to scientific literature identifying some of the difficulties involved in predicting protein function, the Examiner rejected the pending claims on the ground that the applicant cannot impute utility to the claimed invention based on its 97% homology to mouse Vps45. The Examiner's rejection is both incorrect as a matter of fact and as a matter of procedural law.

As demonstrated in § III.B.1., *supra*, the literature cited by the Examiner is not inconsistent with the Applicants' proof of homology by a reasonable probability. It may show that Applicants cannot prove function by homology with **certainty**, but Applicants need not meet such a rigorous standard of proof. Under the applicable law, once the applicant demonstrates a *prima facie* case of homology, the Examiner must accept the assertion of utility to be true unless the Examiner comes forward with evidence showing a person of ordinary skill would doubt the asserted utility could be achieved by a reasonable probability. *See In re Brana*, 51 F.3d at 1566; *In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). The Examiner has not made such a showing and, as such, the Examiner's rejection should be withdrawn.

D. By Requiring the Patent Applicant to Assert a Particular or Unique Utility, the Patent Examination Utility Guidelines and Training Materials Applied by the Patent Examiner Misstate the Law

There is an additional, independent reason to withdraw the rejections: to the extent the

rejections are based on Revised Interim Utility Examination Guidelines (64 FR 71427, December 21, 1999), the final Utility Examination Guidelines (66 FR 1092, January 5, 2001) and/or the Revised Interim Utility Guidelines Training Materials (USPTO Web site www.uspto.gov, March 1, 2000), the Guidelines and Training Materials are themselves inconsistent with the law.

The Training Materials, which direct the Examiners regarding how to apply the Utility Guidelines, address the issue of specificity with reference to two kinds of asserted utilities: "specific" utilities, which meet the statutory requirements, and "general" utilities, which do not. The Training Materials define a "specific utility" as follows:

> A [specific utility] is *specific* to the subject matter claimed. This contrasts to *general* utility that would be applicable to the broad class of invention. For example, a claim to a polynucleotide whose use is disclosed simply as "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

The Training Materials distinguish between "specific" and "general" utilities by assessing whether the asserted utility is sufficiently "particular," *i.e.*, unique (Training Materials at page52) as compared to the "broad class of invention." (In this regard, the Training Materials appear to parallel the view set forth in Stephen G. Kunin, Written Description Guidelines and Utility Guidelines, 82 J.P.T.O.S. 77, 97 (Feb. 2000) ("With regard to the issue of specific utility the question to ask is whether or not a utility set forth in the specification is *particular* to the claimed invention.").)

Such "unique" or "particular" utilities never have been required by the law. To meet the utility requirement, the invention need only be "practically useful," *Natta*, 480 F.2d 1 at 1397, and confer a "specific benefit" on the public. *Brenner*, 383 U.S. at 534. Thus incredible "throw-away" utilities, such as trying to "patent a transgenic mouse by saying it makes great snake food," do not meet this standard. Karen Hall, Genomic Warfare, The American Lawyer 68 (June 2000) (quoting John Doll, Chief of the Biotech Section of USPTO).

This does not preclude, however, a general utility, contrary to the statement in the Training Materials where "specific utility" is defined (page 5). Practical real-world uses are not

limited to uses that are unique to an invention. The law requires that the practical utility be "definite," not particular. *Montedison,* 664 F.2d at 375. Appellant is not aware of any court that has rejected an assertion of utility on the grounds that it is not "particular" or "unique" to the specific invention. Where courts have found utility to be too "general," it has been in those cases in which the asserted utility in the patent disclosure was not a practical use that conferred a specific benefit. That is, a person of ordinary skill in the art would have been left to guess as to how to benefit at all from the invention. In *Kirk*, for example, the CCPA held the assertion that a man-made steroid had "useful biological activity" was insufficient where there was no information in the specification as to how that biological activity could be practically used. *Kirk*, 376 F.2d at 941.

The fact that an invention can have a particular use does not provide a basis for requiring a particular use. *See Brana, supra* (disclosure describing a claimed antitumor compound as being homologous to an antitumor compound having activity against a "particular" type of cancer was determined to satisfy the specificity requirement). "Particularity" is not and never has been the *sine qua non* of utility; it is, at most, one of many factors to be considered.

As described *supra*, broad classes of inventions can satisfy the utility requirement so long as a person of ordinary skill in the art would understand how to achieve a practical benefit from knowledge of the class. Only classes that encompass a significant portion of nonuseful members would fail to meet the utility requirement. *Supra* § III.C.2. (*Montedison,* 664 F.2d at 374-75).

The Training Materials fail to distinguish between broad classes that convey information of practical utility and those that do not, lumping all of them into the latter, unpatentable category of "general" utilities. As a result, the Training Materials paint with too broad a brush. Rigorously applied, they would render unpatentable whole categories of inventions heretofore considered to be patentable, and that have indisputably benefitted the public, including the claimed invention. *See supra* § III.C.2. Thus the Training Materials cannot be applied consistently with the law.

IV. Rejection of Claims 1, 2, 16, and 17 Under 35 U.S.C. § 112, second paragraph

The Examiner rejected Claims 1, 2, 16, and 17 under 35 U.S.C. § 112, second paragraph, alleging that they are "indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention." (Office Action, page 8.)

The MPEP provides that:

> a full explanation of the deficiency of the claims should be supplied Whenever possible, identify the particular term(s) or limitation(s) which render the claim(s) indefinite and state why such term or limitation renders the claim indefinite. If the scope of the claimed subject matter can be determined by one having ordinary skill in the art, a rejection using this form paragraph would not be appropriate. (MPEP, 8th Edition, August 2001, 706.03(d) Rejections Under 35 U.S.C. 112, Second Paragraph)

Therefore claims must be examined on the basis of whether one having ordinary skill in the art would be able to determine the scope of the claim and, if a rejection is made, provide reasons why the claim is indefinite.

The Examiner's rejection had five bases (A, B, C, D, and E), which are addressed separately below.

A. Claim 1(b)

The Examiner alleged that the phrase "a naturally-occurring amino acid sequence having at least 90% sequence identity to" in part (b) of Claim 1 rendered the claim indefinite. The Examiner stated that "Applicants do not describe what is encompassed by the term 'naturally-occurring'. The term 'having . . . sequence identity' does not clearly define the scope of the claim." (Office Action, page 8, emphasis in Office Action.)

Applicants submit that the Examiner has not provided any reasons or evidence why the cited phrase is indefinite and/or why one having ordinary skill in the art could not determine the scope of the claim. For this reason alone, the rejection as directed to Claim 1(b) is improper and should be withdrawn.

Applicant submits that the recitation of "naturally occurring amino acid sequence" in Claim 1 defines **where to find** the amino acid sequences encompassed by the claim. The use of the term "naturally-occurring" distinguishes an amino acid sequence that occurs in nature from synthetic or engineered amino acid sequences that are created through manual genetic manipulations. The term "naturally occurring amino acid sequence" thus defines the origin of the amino acid sequence (i.e., even though one could theoretically make the polypeptides having

at least 90% sequence identity to SEQ ID NO:1 in the laboratory by randomly mutating the human sequence to form a "mutein," the recited "naturally occurring amino acid sequence" must be one that is found in nature). One skilled in the art would understand the meaning of the term "naturally-occurring amino acid sequence" within the context of Claim 1. Moreover, this is standard claim language in claims drawn to polypeptides and polynucleotides, and its use in the instant Claim 1 is entirely consistent with its use in numerous issued U.S. patents, including those of the assignee Incyte as well as in patents of others. Applicants thus request that the rejection be withdrawn.

The Examiner also alleges that the "term 'having . . . sequence identity' does not clearly define the scope of the claim." (Office Action, page 8.) Applicants submit that the phrase "having 90% sequence identity" would be understood by one of ordinary skill in the art.

In evidence of this, Applicants cite Barton et al. (Protein Structure Prediction, A Practical Approach, IRL Oxford University Press, pages 31-63; Reference No. 7) who state that:

> 2.1 Identity scoring
> This is the simplest scoring scheme: amino acid pairs are classified into two types; identical and non-identical. Non-identical pairs are scored zero and identical pairs are given a positive score (usually one). The scoring scheme is generally considered less effective than schemes that weight non-identical pairs, particularly for the detection of weak similarities (2,3). The normalized sum of identity scores for an alignment is popularly quoted as 'percentage identity', . . . (Barton et al., bottom of page 31 through top of page 32.)

Applicants describe the similarity between sequences in Claim 1(b) in terms of "having 90% sequence identity," a term that has a popular meaning according to the Barton reference, published in 1996, prior to the filing of the parent application to the instant case. In addition, the term "having" has a well-known meaning. See Merriam-Webster's Collegiate Dictionary (on-line; Reference No. 8): to have: to be marked or characterized by (a quality, attribute, or faculty).

For at least these reasons, Applicants submit that the phrase "having 90% sequence identity" would be well understood by one of ordinary skill in the art.

B. Claim 1(c)

The Examiner alleged that "Claim 1(c) is indefinite because of the limitation 'a biologically-active fragment of an amino acid sequence. . . '. It is unclear which amino acids

form biologically-active fragments of SEQ ID NO:1 or how the activity would be determined." (Office Action, page 9, emphasis in Office Action.)

The Specification defines "biologically active" on page 8, line 30 through page 9, line 1 and an assay method is described in Example X, page 54, lines 14-21, and in addition, assays are described in the art, e.g., in Tellam, et al. (Reference No. 2).

C. Claim 1(d)

The Examiner alleged that "Claim 1(d) is indefinite because of the limitation 'an immunogenic fragment of an amino acid sequence . . .'. It is unclear which amino acids form immunogenic fragments of SEQ ID NO:1." (Office Action, page 9, emphasis in Office Action.)

The Specification defines "immunologically active" on page 9, lines 1-4 and "immunogenic" on page 30, line 22 through page 31, line 3 and page 54, line 24 through page 55, line 9.

D. Claim 2

The Examiner alleged that "Claim 2 is indefinite because of the limitation '. . . having a sequence. . . '. The term 'having a sequence' does not clearly define the scope of the claim." (Office Action, page 9.)

Applicants submit that the Examiner has not provided any reasons or evidence why the cited phrase is indefinite and/or why one having ordinary skill in the art could not determine the scope of the claim. For this reason alone, the rejection as directed to Claim 2 is improper and should be withdrawn.

In addition, the MPEP (8th Edition, August 2001, Section 2111.03) states that

> Transitional phrases such as "having" must be interpreted in light of the specification to determine whether open or closed claim language is intended. See, e.g., *Lampi Corp. v. American Power Products Inc.*, 228 F.3d 1365, 1376, 56 USPQ2d 1445, 1453 (Fed. Cir. 2000) (The term "having" was interpreted as open terminology, allowing the inclusion of other components in addition to those recited); *Crystal Semiconductor Corp. v. TriTech Microelectronics Int'l Inc.*, 246 F.3d 1336, 1348, 57 USPQ2d 1953, 1959 (Fed. Cir. 2001) (term "having" in transitional phrase "does not create a presumption that the body of the claim is open"); *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1573, 43 USPQ2d 1398, 1410 (Fed. Cir. 1997) (In the context of a cDNA having a

sequence coding for human PI, the term "having" still permitted inclusion of other moieties.).

However, in order to expedite prosecution, amended Claim 2 recites "[a]n isolated polypeptide of claim 1, comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5."

E. Claim 17

The Examiner alleged that "Claim 17 is indefinite because of the limitation '. . . polypeptide has an amino acid sequence . . . '. The term 'has a sequence' does not clearly define the scope of the claim." (Office Action, page 9, emphasis in Office Action.)

Applicants again submit that the Examiner has not provided any reasons or evidence why the cited phrase is indefinite and/or why one having ordinary skill in the art could not determine the scope of the claim. For this reason alone, the rejection as directed to Claim 17 is improper and should be withdrawn. Applicants refer the Examiner to the portion of MPEP Sections 706.03(d) and 2111.03 cited above.

However, in order to expedite prosecution, amended Claim 17 recites "[a] composition of claim 16, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5."

For at least the above reasons, Applicants respectfully request that the Examiner withdraw the § 112, second paragraph rejection of Claims 1, 2, 16, and 17.

V. Rejection of Claims 1 and 2 Under 35 U.S.C. § 102(b) as Being Anticipated by Pevsner et al.

The Examiner rejected Claims 1 and 2 under 35 U.S.C. § 102(b) "as being anticipated by Pevsner et al. (EMBL sequence with accession number ACQ15715, 'Vacuolar protein sorting homolog h-vps45' November 1, 1996)." (Office Action, page 9.)

To expedite prosecution of the application, Claim 1 has been amended to recite "a naturally-occurring amino acid sequence having at least 98% sequence identity to the amino acid sequence of SEQ ID NO:1." Naturally-occurring amino acid sequences having at least 98%

sequence identity to an amino acid sequence of SEQ ID NO:1 are supported in the Specification, e.g, at page 14, lines 26-29. ("As shown in Figures 2A and 2B, VTP-1 has chemical and structural homology with a mouse vacuolar protein-sorting protein, mVps45 (GI 1703494; SEQ ID NO:7). In particular, VTP-1 and mVps45 share 97% sequence homology.")

The Pevsner et al. document does not recite a polypeptide having at least 98% sequence identity to an amino acid sequence of SEQ ID NO:1. Therefore, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1 and 2 under 35 U.S.C. § 102(b) as being anticipated by Pevsner et al.

CONCLUSION

Applicants respectfully submit that rejections for lack of utility based, *inter alia*, on an allegation of "lack of specificity," as set forth in the Office Action and as justified in the Revised Interim and final Utility Guidelines and Training Materials, are not supported in the law. Neither are they scientifically correct, nor supported by any evidence or sound scientific reasoning. These rejections are alleged to be founded on facts in court cases such as *Brenner* and *Kirk*, yet those facts are clearly distinguishable from the facts of the instant application, and indeed most if not all nucleotide and protein sequence applications. Nevertheless, the PTO is attempting to mold the facts and holdings of these prior cases, "like a nose of wax,"[2] to target rejections of claims to polypeptide and polynucleotide sequences, as well as to claims to methods of detecting said polynucleotide sequences, where biological activity information has not been proven by laboratory experimentation, and they have done so by ignoring perfectly acceptable utilities fully disclosed in the specifications as well as well-established utilities known to those of skill in the art. As is disclosed in the specification, and even more clearly, as one of ordinary skill in the art would understand, the claimed invention has well-established, specific, substantial and credible utilities. The rejections are, therefore, improper and should be withdrawn.

Moreover, to the extent the above rejections were based on the Revised Interim and final Examination Guidelines and Training Materials, those portions of the Guidelines and Training Materials that form the basis for the rejections should be determined to be inconsistent with the law.

Applicants also request the withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, and 35 U.S.C. § 102(b).

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

---

[2]"The concept of patentable subject matter under §101 is not 'like a nose of wax which may be turned and twisted in any direction * * *.' *White v. Dunbar*, 119 U.S. 47, 51." *(Parker v. Flook,* 198 USPQ 193 (US SupCt 1978))

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent at (650) 845-4646.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: January 14, 2002

Susan K. Sather

Susan K. Sather
Reg. No. 44,316
Direct Dial Telephone: (650) 845-4646

3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886